



## Case Report

## Concurrent diagnosis of infective endocarditis and acute rheumatic fever: A case report



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## ABSTRACT

Rheumatic heart disease has been classically considered as a risk factor for infective endocarditis (IE). Although valvulitis is frequently present in patients with acute rheumatic fever (ARF), the established valve disease after initial episode of ARF is usually considered as a predisposing factor for IE. We hereby present a biopsy-proven case of IE co-diagnosed with the first episode of ARF.

**<Learning objective:** Infective endocarditis and acute rheumatic fever are both diagnosed with clinical criteria. When both of these conditions are possible in a single case, however, the diagnosis might be challenging. We highlight this issue in the presented case.>

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## Introduction

Infective endocarditis (IE) is an infection of the endocardial surface of the heart with a mortality rate as high as 25%. Despite significant developments in the prophylaxis of IE in recent decades, its rate of incidence has been nearly constant that means a change in the profile of IE risk factors during the time. However, in contrast to high-income countries, most cases of IE among low-income societies have remained related to classic risk factors such as rheumatic heart disease.

Rheumatic heart disease and acute rheumatic fever (ARF), a delayed sequela of immunologic response to the group A streptococcal pharyngitis, are the leading causes of cardiovascular death during the first five decades of life in developing countries [1]. Diagnosed clinically by revised Jones criteria [2], ARF patients frequently have valvulitis at first episode. Nevertheless, chronic and established valve disease after recovery from the initial episode of ARF is usually considered as a predisposing factor for IE.

Although valvulitis is frequently present in patients with ARF, chronic and established valve disease after recovery from the

initial episode of ARF is usually considered as a predisposing factor for IE. We hereby report a case of IE from Iran that concurrently occurred with the first episode of ARF.

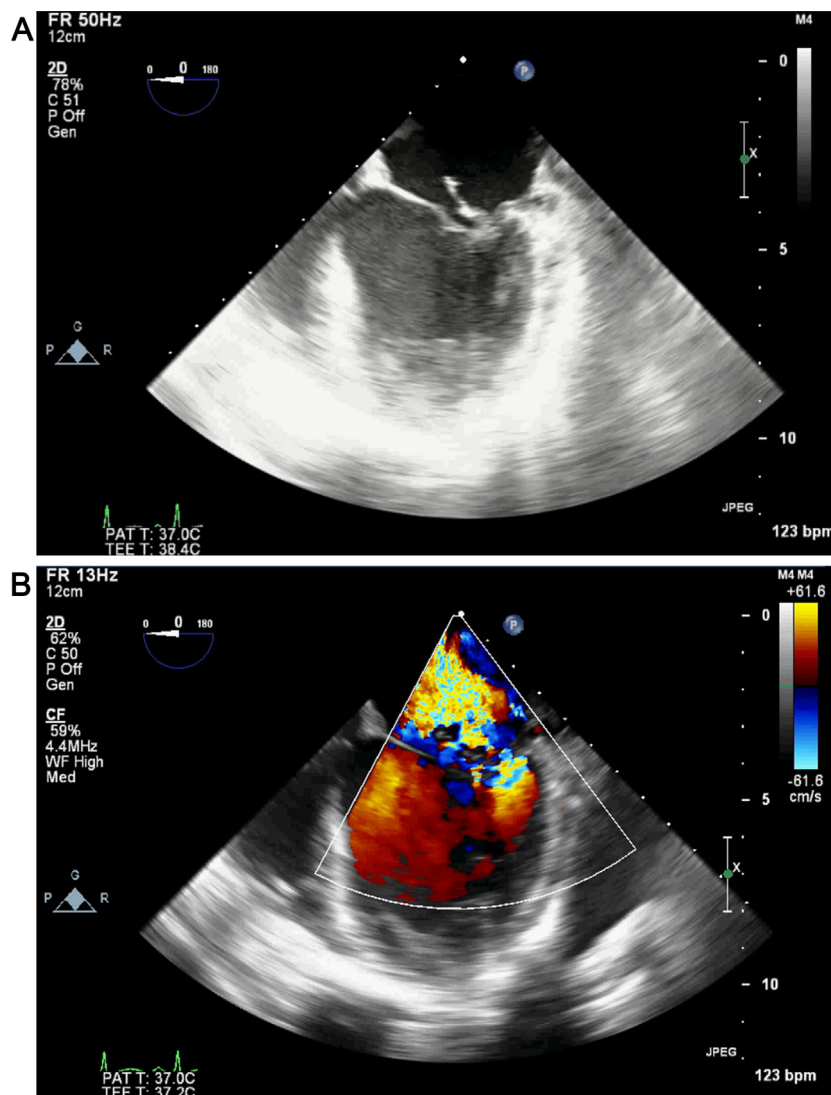
## Case report

A 13-year-old girl was seen in our hospital for fever and palpitation. She had been in her usual state of health until 7 weeks earlier when malaise, body pain, and influenza-like symptoms developed. She then visited her physician and with some symptomatic treatments a partial relief was achieved. Four weeks later she had an outpatient visit for anorexia, subjective fever, and exertional dyspnea. Reportedly, a set of laboratory tests was requested and a course of antibiotic therapy (at first parenterally; later orally) was started. During the 2 weeks of taking antibiotics she missed follow-up appointments because of subjective sense of relief and defervescence. A week later she was brought to our center.

The patient had no past history of congenital heart disease. At physical examination, she was febrile (oral temperature: 38.9 °C) with heart rate of 145 beats per minute, the rest of vital signs being normal. There was a IV/VI holosystolic murmur at the cardiac apex with radiation to the axilla. The spleen edge was palpable at 5 cm below the costal margin. High erythrocyte sedimentation rate (ESR = 65 mm/h) and C-reactive protein [CRP = 26 mg/dL (normal

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**Fig. 1.** Patient's 2-dimensional (A) and color Doppler (B) echocardiography images showing mitral valve vegetation and regurgitation.

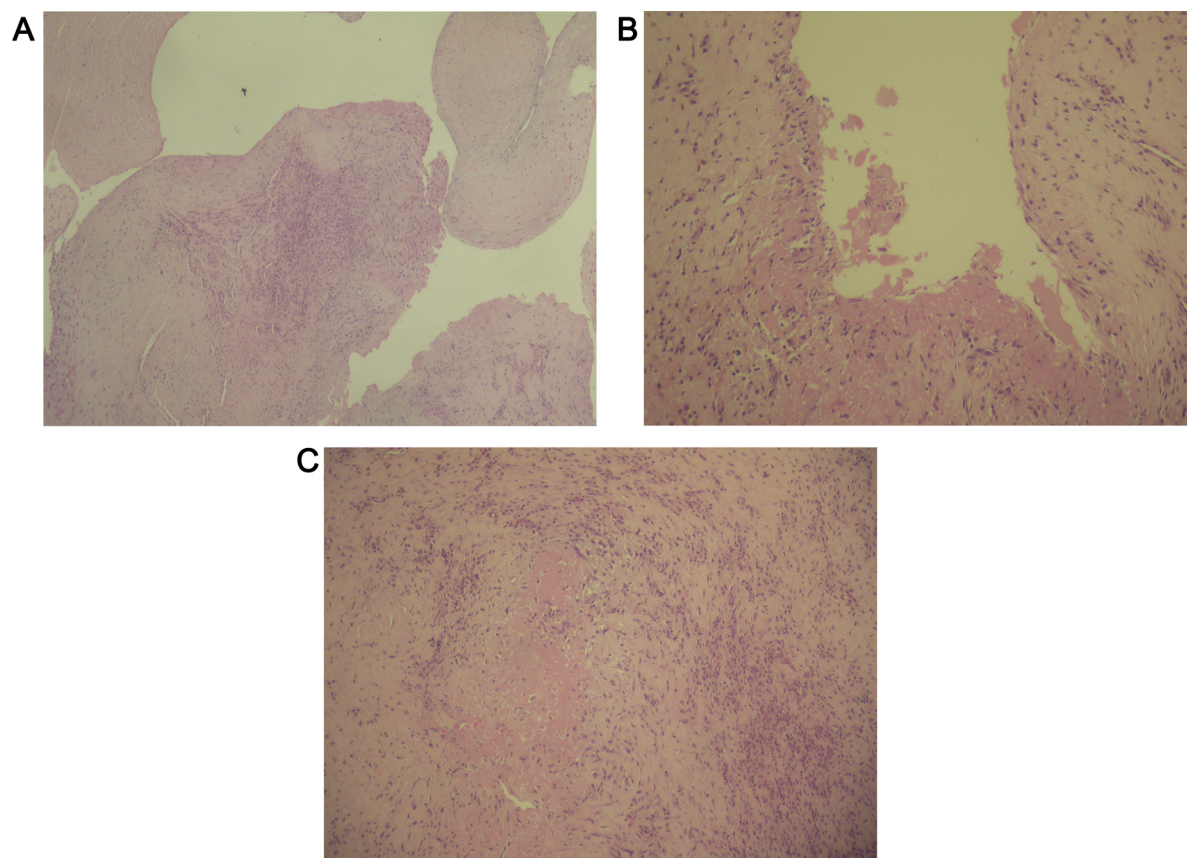
range: <6 mg/dL)], normocytic anemia (hemoglobin: 8 gr/dL), and borderline leukopenia (white blood cell: 4100/mcL) were found at hematology test. Abdominopelvic sonography and computed tomography (CT) scan confirmed splenomegaly and demonstrated a 21 × 15 mm splenic abscess. Trans-esophageal echocardiography (TEE) revealed an 18 mm mobile, strand-like mass attached to the posterior mitral valve leaflet (PMVL), protruded to the left atrium, and perforated the PMVL, resulting in severe mitral regurgitation from the perforation; and moderate systolic dysfunction (ejection fraction: 40–45%) regarding the severity of mitral regurgitation (Supplementary Video S1, Fig. 1).

Empiric antibiotic therapy with ampicillin-sulbactam (3 gr, q6h) plus vancomycin (1 gr, q12h) was started and surgical repair was planned. At surgery, the remnant of vegetation and the perforated P1 segment of PMVL were resected, then repaired by a pericardial patch. Histopathological examination of the vegetation demonstrated polymorphonuclear and lymphoplasmic cells in valve which was in favor of IE and confirmed the clinical diagnosis, but, surprisingly, areas composed of fibrinoid bodies surrounded by epithelioid histiocytes forming granuloma, namely “Aschoff bodies”, were found at the resected segment of mitral valve that was compatible with pathological diagnosis of ARF (Fig. 2). None of

the surgical specimens or blood cultures had positive culture results. However, after 1 week of hospitalization, a positive culture result for *Streptococcus pyogenes* was received from the patient's blood sample taken 4 weeks earlier as an out-patient. The patient's post-operative clinical course was uneventful and she was discharged home after a total 6 weeks of intravenous antibiotic therapy.

## Discussion

In the present case, based on the preoperative background clinical context (continuing fever + constitutional symptoms) and CT findings (splenic abscess), the TEE results were considered as compatible with a complicated IE; and the patient received surgical treatment along with intravenous antibiotics. Since histopathology of the vegetation revealed active endocarditis, this patient represents a definite case of IE according to the well-accepted Duke Criteria [3]. Negative culture results in our center, however, probably resulted from previous administration of antibiotics. Regarding the *S. pyogenes* derived from blood samples before antibiotic therapy, although it is not a typical agent for IE,



**Fig. 2.** Vegetation of mitral valve containing inflammatory cells in favor of infective endocarditis (A); and granulomatous structures with peripheral epithelioid histiocytes (B) and fibrinoid change (B,C), Aschoff body, in favor of acute rheumatic fever.

many cases of IE owing to that microorganism have already been reported in the literature [4–6]. Those and our case share some features as follows:

1. IE occurring in a structurally normal heart – in the majority of cases of IE due to *S. pyogenes* there was no structural heart disease as a risk factor [4–6].
2. Involvement of the left heart – in almost all reports among non-injection drug users, the involved valves have been mitral or aortic [4–6].

The most common portal of entry for *S. pyogenes* bacteremia in children is pharyngitis or skin lesions. In this case, according to the initial influenza-like symptoms, the primary source of bacteremia has likely been pharyngitis. If one accepts that a clinical diagnosis of pharyngitis has been neglected at the beginning of the disease course, the occurrence of ARF within the following weeks is likely. Considering the revised version of the well-known Jones criteria [2], however, the patient has had none of the major clinical manifestations of ARF preoperatively, except for a subclinical carditis – if any. Absence of arthritis, which is the most common major manifestation of ARF, might have resulted from blind prescription of nonsteroidal anti-inflammatory drugs for symptomatic treatment of the patient's constitutional symptoms early in the course of her disease. Yet, absence of clinical features suggesting valvular damage in ARF (the so-called “subclinical” carditis) has been well noted worldwide [7]. Some minor manifestations of ARF, such as fever and high ESR, were present in our case prior to the surgery; but those are also seen in cases of IE.

Keeping those points in mind, the pre-operative diagnosis of IE was considered in this patient that was then confirmed by microscopic evaluation of the vegetation specimen. Nonetheless, “Aschoff bodies” observed at the histopathological examination of the specimen from the mitral valve was definitely in favor of ARF; according to the literature, Aschoff body is pathognomonic for rheumatic carditis, namely ARF [8]. Therefore the final diagnosis for this case was IE + ARF. Accordingly, we think a neglected streptococcal pharyngitis was the primary event in this patient, after which the autoimmune process of ARF was started; and the subsequent ‘inflammatory’ carditis was then more complicated by an ‘infectious’ event – IE with the same organism.

Recently, Suzuki et al. [9] reported a case with concurrent diagnosis of IE and ARF and reviewed the literature for similar reports. Although in that case, a 68-year-old woman with aortic valve vegetation, the clinical criteria for both IE and ARF had been fulfilled preoperatively, the histopathological examination of the aortic valve specimen failed to detect Aschoff bodies; but just demonstrated “massive neutrophil infiltration with fibrin deposition” as a clue for “strong inflammation” such as IE. Moreover, according to their review of the literature, 12 of the 21 cases of Group A streptococcal IE were also diagnosed with ARF based on the 1992 update of Jones criteria. Nonetheless, only in two of those cases the pathology information has been reported, both of which were just in favor of IE not ARF.

Çetin et al. [10] also reported a teenage girl with mitral valve vegetation along with (severe) mitral and (mild) aortic regurgitation, whose final diagnosis was concurrent IE and ARF. The diagnosis of both IE and ARF in that case was also made only by

clinical criteria (the Duke criteria and the modified Jones criteria) and no histopathological confirmation was performed.

In conclusion, we hereby presented a case with histopathologically confirmed co-diagnosis of IE and ARF, suggesting such a potential for *S. pyogenes* to cause both disorders simultaneously in a single patient. To the best knowledge of the authors, this is the first report with pathologic findings of both IE and ARF in a single case.

### Conflict of interest

The authors declare that there is no conflict of interest.

### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.jccase.2017.12.011>.

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